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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/740,486 | 12/19/2000 | Alan S. Waggoner | 92053CONCIPCON | 6161 |

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EXAMINER

PONNALURI, PADMASHRI

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| | 1639 |

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

| | | | |
|-----------------|---------------------|--------------|-------------------|
| Application No. | 09/740,486 | Applicant(s) | WAGGONER, ALAN S. |
| Examiner | Padmashri Ponnaluri | Art Unit | 1639 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 9/16/04.
2a) This action is FINAL. 2b) This action is non-final.
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 25-29 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) Claim(s) _____ is/are allowed.
6) Claim(s) 25-29 is/are rejected.
7) Claim(s) _____ is/are objected to.
8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/15/04.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. 102004.
5) Notice of Informal Patent Application (PTO-152)
6) Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/16/04 has been entered.
2. The amendment filed on 6/28/04 has been fully considered and entered into the application.

Status of claims

3. Claims 9-12, 15, 19, 21-24 have been canceled by the amendment filed on 6/28/04. Claims 25-29 are currently pending and are being examined in this application.

Information Disclosure Statement

4. The references filed in the information disclosure statement have been fully considered.
filed on 9/15/04,
A

Response to Amendment

5. The declaration under 37 CFR 1.132 filed on 9/16/04 is sufficient to overcome the rejection (35 USC 102 (b)/ 103) of claims 25-29 based upon US Patent 4,404,289 (MASUDA et al) or US Patent 4,405,711 (MASUDA et al).

New rejections

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by either US Patent either US Patent 4,404,289 (MASUDA et al) or US Patent 4,405,711 (MASUDA et al).

Masuda et al (the '289 patent) disclose methods for immunochemical measurement of trace component. The reference discloses that the antigen or antibody (refers to protein or component of the instant claims) labeled with spectral sensitizers such as cyanine dyes of formula C (i.e., see column 10) (refers to the water soluble dye of the instant claims). The reference discloses that the disclosed spectral sensitizers are particularly advantageous as the labeling substances since these dyes are excellent in binding to the trace components such as antigen or antibody. The reference discloses the cyanine dye of formula C in columns 11-13. The reference discloses that merocyanine dyes (M') or cyanine dyes (C') are introduced into the antigen or antibody via covalent bond (i.e., see column 14). The reference discloses that both the spectral sensitizers and the antigen or antibody contain either an amino group, a carboxy group, a carboxylic group or a hydroxy group, and linking between functional groups of antigen or antibody and the functional groups of spectral sensitizers (i.e., see column 14).

The reference discloses that the cyanine dye of formula C and water (refers to the water soluble dye of the instant claim) is used in labeling insulin (a protein) (e.g., example 1), lysozyme (e.g., example 2). The reference discloses that the insulin labeled with spectral sensitizer (I) has absorption spectrum of 660 nm (within the '400-900 nm range' of absorption of the instant claim dye). The reference discloses that the amount of spectral sensitizer used for labeling varies depending upon the kind of substances to be labeled, but is generally in a molar ratio of 1/100 to 100 moles per 1 mole of antigen or antibody.

Masuda et al (the '711 patent) discloses a method of assay for a trace component such as antigen, antibody or enzyme utilizing immunochemical reaction or enzyme reaction in combination with photographic detection system comprising optical density. The reference discloses that the spectral sensitizer employed for labeling a trace component such as antigen or antibody or synthetic substrate, include cyanine dyes (i.e., see column 10) (refers to the water soluble dye of the instant claims).

Masuda et al (the '289 patent and the '711 patent) teach cyanine dyes and the use of the dyes to label antigen or antibody or proteins. The references clearly anticipate the claimed invention.

Maintained Claim Rejections

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 25-28 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Waggoner et al (Biophysical Journal, vol. 33, 1981, page 292a) for the reasons set forth in the previous office action mailed on 1/23/04.

Waggoner et al disclose that the reactive sulfhydryl group on the F1 region of cattle rhodopsin (chromoprotein) (refers to the instant claim component) has been covalently labeled with a cyanine dye (refers to the instant claim dye). The absorption of the dye at 660 nm is sensitive to conformational changes of rhodopsin that occur following a short and intense light flash. The reference discloses labeled detergent solution of rhodopsin (refers to soluble dye of the instant claims).

Waggoner et al do not teach that the 'individual dye molecule has an average molar extinction coefficient of at least 50,000 liters per mole centimeter, an average quantum yield of at least 5 percent...' The claimed invention further differs from the prior art teachings only by the recitation of properties of the cyanine dyes (individual dye molecule has an average molar extinction coefficient of at least 50,000 liters per mole centimeter, an average quantum yield of at least 5 percent). However Waggoner et al teach cyanine dyes which read on the instant claimed dyes. The reference teaches the same dyes of the instant claim composition, and the dye has the absorption range within the claimed range of 400-900 nm (the absorption of the reference dye is at 660 nm, within the claimed range). Thus the claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific properties of the instant composition versus the reference composition. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed composition has a different dye from the one taught by prior art and to establish the patentable differences. See *in re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922(PTO Bd.Pat. App. & Int. 1989).

10. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 3,148,187 (Heseltine et al) and US Patent 4,404,289 (Masuda et al).

NOTE this rejection is same as the 35 USC 103 rejection of claims 25-29 (in paragraph 13, of the office action mailed on 1/23/04).

US Patent 3,148,187 (Heseltine et al) teaches sulfonated cyanine and merocyanine dyes.

The reference teaches nuclear sulfonated dyes. The reference teaches the nuclear sulfo-substituted dyes of the invention include cyanine dyes of formula I. The reference teaches the methods of sulfonating the cyanine dyes. The reference teaches that the sulfonated dyes are valuable for use in photography because of their good solubility in water (see column 6). The reference teaches the soluble dyes are prepared by direct nuclear sulfonation of cyanine dyes. The reference teaches that the dyes prepared by the method are distinguished from the prior art dyes by having at least one sulfo group attaches to a nuclear carbon atom rather than a nitrogen atom in the heterocyclic ring (i.e., see column 6). The reference sulfonated cyanine dyes read on the cyanine dyes of the instant claim. The claimed invention differs from the prior art teachings by reciting that the component has at least one amino or hydroxy group, which reacts with the cyanine dye.

The claimed invention differs from the prior art teachings by reciting 'dye labeled component.' US Patent 3,148,187 (Heseltine et al) teaches cyanine dyes useful in photography. The reference recites water soluble cyanine dyes. The reference does not teach that the cyanine dyes are used in labeling biological compounds. However Masuda et al teach methods for immunochemical measurement of trace component. The reference teaches that the antigen or antibody (refers to protein or component of the instant claims) labeled with spectral sensitizers such as cyanine dyes of formula C (i.e., see column 10) (refers to the water soluble dye of the instant claims). The reference teaches that the disclosed spectral sensitizers are particularly advantageous as the labeling substances since these dyes are excellent in binding to the trace components such as antigen or antibody. The reference teaches cyanine dye of formula C in

columns 11-13. The reference discloses that the cyanine dye of formula C and water (refers to the water soluble dye of the instant claim) is used in labeling insulin (a protein) (e.g., example 1), lysozyme (e.g., example 2). The reference teaches that the insulin labeled with spectral sensitizer (I) has absorption spectrum of 660 nm (within the '400-900 nm range' of absorption of the instant claim dye). The reference discloses that the amount of spectral sensitizer used for labeling varies depending upon the kind of substances to be labeled, but is generally in a molar ratio of 1/100 to 100 moles per 1 mole of antigen or antibody.

Thus it would have been obvious to one skilled in the art to use the water soluble cyanine dyes taught by the reference US Patent 3,148,187 (Heseltine et al) or Masuda et al with the method of labeling antigen or antibody taught by US Patent 4,404,289 because US Patent 3,148,187 (Heseltine et al) teaches the advantages of the water soluble sulfonated cyanine dyes and the '289 teaches the advantages of the use of spectral sensitizers in labeling the antigen or antibody. A person skilled in the art would have been motivated to obtain the cyanine dye labeled compounds such that labeled compounds are useful in diagnostic assays which would enable one to reduce the quantity of a testing sample required for improved detection sensitivity and thus enables multiple test samples.

Response to Arguments

11. Applicant's arguments filed 6/28/04, regarding the rejection of claims 25-28 over Waggoner et al have been fully considered but they are not persuasive.

Applicants argue that the Waggoner reference lacks the features of claims 25 and 26, i.e.,

that the cyanine dye must have a molar extinction coefficient of at least 50,000 liters, have an average quantum yield of at least 5 percent and must absorb and emit in the 400 to 900 nm range when photostable reaction product is in aqueous environment.'

Applicant's arguments have been fully considered and are not persuasive, since the reference (Waggoner et al) teaches cyanine dyes used in labeling proteins. And applicant's arguments are based on the properties of the cyanine dye used or conjugated to the protein. Since the reference teaches cyanine dye, and used in labeling, and has absorbance of 660 nm, which is within the claimed range (400-900 nm), it is considered that the cyanine dye of the reference is same or obvious variations of the reference teachings, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific properties of the instant composition versus the reference composition. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed composition has a different dye from the one taught by prior art and to establish the patentable differences. See *in re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922(PTO Bd.Pat. App. & Int. 1989).

Applicant's arguments regarding the rejection of claim 29 over Waggoner et al reference has been considered, however the arguments are moot since the rejection has not included claim 29.

12. Applicant's arguments filed on 6/28/04, regarding the rejection of claim 29 over US patent 3,148,187 (Heseltine et al) and US Patent 4,404,289 (Masuda et al), have been fully considered but they are not persuasive.

Applicants argue that Heseltine teaches sulphonated cyanine and merocyanine dyes that

are useful in photography. However, Heseltein does not teach cyanine dyes that are useful in labeling biological compounds for the reasons explained above.

In response to applicant's argument that 'useful for labeling biological compounds', a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants arguments regarding the 'luminescence detection', is considered as intended use; and since the reference cyanine dyes has absorbance within the claimed range, thus the reference cyanine dyes are considered to have the properties 'luminescence properties of the compounds.' If applicants believe that the cyanine dyes of the reference are structurally and functionally distinct from the claimed dyes, applicants are requested to either include the structural features, which are different or provide a declaration showing that the reference compounds are different.

Further the joint declaration by Burrows and West do not overcome the obviousness rejection of claim 29 because claim 29 is independent claim, and do not have same limitations as

claim 25. And the declaration shows that the cyanine dyes of the reference (Masuda et al) do not have the same solubility, fluorescence properties as the claimed cyanine dyes. However, the instant claim 29 does not recite any of the properties of the cyanine dyes, thus rejections have been maintained.

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639


PADMASHRI PONNALURI
PRIMARY EXAMINER

22 November 2004.